

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/7/2010 has been entered.

Claims 2, 3, 14 and 15 are canceled, claims 1, 4-12, 25 and 28 are withdrawn from consideration as being drawn to non-elected subject matter, and claims 13, 16-24, 26 and 27 have been considered on the merits. All arguments have been fully considered.

Response to Arguments

Applicant's arguments filed 1/7/2010 have been fully considered but they are not persuasive.

Applicant alleged that it is not obvious to a person of ordinary skill in the art to use the apparatus to maintain undifferentiated, proliferating hES cells by applying strain. Applicant is reminded that the currently claimed invention is directed to the cell culture composition (product) comprising hES cells and an apparatus configured to apply a periodic strain rather than a method of using the apparatus in the composition. Patentability of product claims is determined by structure of the product rather than the method of using it.

The structural limitation of the instant invention is considered to be hES cells, unconditioned culture medium, a flexible solid porous matrix without feeder fibroblasts, and the cited references teach these components.

Applicant indicated that it was not clear how maintaining differentiation would have made obvious to one of skill in the art Applicants' cell culture composition of undifferentiated human ES cells. The claim rejection stated that the teaching of Xu combined with that of Russell is the Matrigel, and the rationale of substituting hydrogel of Russell with Matrigel of Xu is an art-recognized alternative and/or equivalent.

The discussion presented in the previous OA was to rebut the applicants' argument based on the intention of Russell's method. Whether or not maintaining differentiated state can be interpreted as merely keeping cells alive as asserted by applicant, the intended purpose of the product would not provide structural limitation to the claimed invention.

Applicant asserted that the ES cells before and after the application of the periodic strains are different such that with strains the ES cells remain undifferentiated whereas without the strains, the ES cells spontaneously differentiate. The Examiner believes that there is significant difference in the behavior of ES cells with and without the application of the periodic strain. However, this difference is only obtainable after applying the method steps of treating hES cells with such periodic strains, but the currently claimed invention is not about method of using the periodic strains in order to keep the hES cells undifferentiated, rather it is interpreted as a composition having undifferentiated hES cells, unconditioned culture medium, a flexible porous matrix, and an apparatus capable of providing a periodic strain, which does not require any active strain applied to the cells.

Applicant alleged that the Examiner's allegation that applying strain has no effect on ES cells would eliminate any motivation for the skilled artisan to combine Russell with Xu. It appears that applicant misinterpreted the Examiner's argument. The Examiner wishes to clarify

the statement which was meant that ES cells should be the same “undifferentiated” state before and after the application of the periodic strain. However, whether or not there is any effect on ES cells, the combination of Russell with Xu is about substitution of hydrogel of Russell with Matrigel without fibroblast feeder cells as taught by Xu, and it is nothing to do with the effect of periodic strains on ES cells.

Applicant asserted that Russell teaches that cell differentiation is accelerated in response to applying strain. Whether or not the Russell’s teaching is related to accelerating differentiation, the intended purpose of the Russell’s method is different from the intended purpose of the claimed product, it does not provide any structural limitation to the claimed product in determining patentability.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13, 16-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al. (US 2002/0081726) in view of Xu et al. (2001).

Russell et al. teach a hES cell culture composition (see paragraph [0106]) grown on hydrogel matrix (see paragraph [0015]), and an apparatus [Flexercell strain system (FX-3000) and BioFlex plate] (see paragraph [0161]) on which the cells are stretched by a vacuum (see paragraph [0146]). Russell et al. also teach the percentage of strain starting at 5% (see paragraph [0179]) and the frequency of strain or pattern of strain can be readily varied by programming the

system (see paragraph [0146]).

While Russell et al. teach hES cells and hydrogel, Russell et al. do not teach the hES cells on Matrigel (flexible porous matrix) without fibroblast feeder cells.

Xu et al. teach a culture of human embryonic stem (hES) cells on Matrigel without fibroblast feeder cells (see Abstract and Fig. 1). Xu et al. also teach undifferentiated hES cells on Matrigel in non-conditioned ES medium (see Fig. 1J). Xu et al. also teach the undifferentiated hES cells are positive for surface markers such as Oct4 and SSEA-4, and also positive for alkaline phosphatase (see Fig.1 and p.972, left column, 2nd paragraph).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute the hydrogel taught by Russell et al. with Matrigel without fibroblast feeder cells taught by Xu et al. because a person of ordinary skill in the art would recognize Matrigel without fibroblast feeder cells would be an art-recognized equivalent matrix to the hydrogel for ES cell culture.

M.P.E.P. §2144.06 states “In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter.

1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. “This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor.” 209 USPQ at 759.).”

With regard to the limitations drawn to the apparatus of the claims being configured to apply mechanical strain, vacuum pressure, or oscillatory stretching to the matrix and the hES cells, or to exert at least about 5% on the matrix or to stretch at least about 6 times per minutes, the apparatus of Russell et al., Flexercell system, is identical to the claimed apparatus and therefore, the apparatus can be configured to carry out the claimed limitations and thus, it renders the claims obvious.

Furthermore, it would have been obvious for a person of ordinary skill in the art because Russell et al. clearly indicates that varying patterns of strain (e.g. sinusoidal, stepwise, sustained, etc) can be readily programmed using factory-installed protocols using Flexercell strain unit (see paragraph [0146]), thus the various strain rate or the mode of stretching used in the claimed invention are result effective variables and effectively modified by programming the unit. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine

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experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651